REMARKS

Entry of the foregoing, reexamination and reconsideration of the subject matter identified in caption, as amended, pursuant to and consistent with 37 C.F.R. §1.112, and in light of the remarks that follow are respectfully requested.

Claims 25-51, 53-81, 83-111 and 113-114 are pending in the application, Claims 2-24 having been canceled at page 2 of the Request for Filing Continuation/Divisional Application filed December 14, 2000, and Claims 52, 82 and 112 having been canceled above.

By the above amendments, Claims 47 and 48 have been amended to include proper Markush format.

Turning now to the Official Action, Claims 17 and 21-23 stand objected to under 37 C.F.R. §1.175 as being improper for being multi-dependent claims that depend from other multi-dependent claims. Additionally, Claims 2-9 stand objected to as being dependent from a canceled claim. As indicated above, because Claims 2-24 were canceled in the Request for Filing Continuation/Divisional Application, these objections are moot.

For at least these reasons, reconsideration and withdrawal of the objections are respectfully requested.

Claims 10-16, 18-20 and 24-114 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. For at least the reasons that follow, withdrawal of these rejections is in order.

With respect to the rejection of Claims 10-16, 18-20 and 24, Applicants submit that because Claims 2-24 were canceled in the Request for Filing Continuation/Divisional Application, the rejections of Claims 10-16, 18-20 and 24 are moot.

With respect to Claims 47 and 48, Applicants have amended Claims 47 and 48 to obviate the rejection. In particular, Applicants have amended Claim 48 by replacing "an agent that affects at least one of skin differentiation, proliferation, and pigmentation" with --a skin differentiation modulating agent, a skin proliferation modulating agent, a skin pigmentation modulating agent--, as set forth in the claims of the parent patent (U.S. Patent No. 6,235,291 B1).

With respect to the rejection of the independent claims as being indefinite for use of the phrase "preventing sensitive skin" and for failing to specify "what is being treated," Applicants have amended independent Claims 25, 55 and 85 to obviate this rejection. In particular, Applicants have deleted the words "or preventing" and have added the words --such sensitive skin having or developing neurogenic manifestations of dysesthesia caused by the release of substance P therein, the method--, as recited in the claims of the parent patent (U.S. Patent No. 6,235,291 B1), to better emphasize the claimed method of treatment.

With respect to the rejection of Claims 28 and 57 as being indefinite for including the words "side effects of dysesthesia" and "side effects of overheating," Applicants respectfully submit that Claims 28 and 57 satisfy the requirements of 35 U.S.C. §112. That is, as explained in the specification at page 2, the symptoms of dysesthesia are "more or less painful sensations in a skin area, e.g., tingling, prickling, itching or pruritus,

burning, overheating, discomfort, tugging sensations, etc." In addition, even though not explicitly explained in the specification, because the term "overheating" is commonly used in the field of dermatology to refer to hot or burning sensations on the skin, Applicants respectfully submit that the use of the words "side effects of overheating" would be readily understood by those of ordinary skill in the art.

With respect to the rejection of Claims 47, 77 and 107 as being indefinite for using the term "allantoin sugars," Applicants have amended Claims 47, 77 and 107 by replacing "allantoin sugars" with --allantoin, sugars--. Support for this amendment can be found at least at page 12, third full paragraph.

With respect to the rejection of Claims 49, 79 and 109, Applicants provide the following remarks. As explained at page 5 of the specification, the present invention is related to the discovery of the use of a substance P antagonist to treat sensitive skin. More specifically, the present invention is directed to the discovery that substance P antagonists can be used in compositions to prevent and/or combat skin irritations, desquamation, erythemas, sensations of overheating or dysesthesia and/or pruritus in the skin. Additionally, the specification at page 12, indicates that the substance P antagonists may be combined with active ingredients that prevent and/or treat skin disorders. That is, because active agents for the treatment of skin disorders can often produce irritating side effects, Applicants discovered that it would be advantageous to combine substance P antagonists with compositions comprising such active ingredients. Accordingly, the presence of an antagonist in a cosmetic composition containing an active ingredient that produces an irritant effect would make it possible to attenuate or eliminate the irritant effect. See

specification at page 14. Thus, Applicants submit that Claims 49, 79 and 109, when read in view of the specification, would be readily understood by those of ordinary skill in the art.

With respect to the rejection of Claims 52, 82 and 112, Applicants have canceled Claims 52, 82 and 112 to obviate the rejection.

Accordingly, reconsideration and withdrawal of the rejections are respectfully requested.

Claims 10-16, 18-20 and 24-105 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-16 of U.S. Patent No. 5,714,155, Claims 1-19 of U.S. Patent No. 5,679,360, Claims 1-10 of U.S. Patent No. 5,788,956, Claims 1-16 of U.S. Patent No. 5,824,650, Claims 1-22 of U.S. Patent No. 5,932,215 and Claims 1-30 of U.S. Patent No. 6,235,291.

In response, Applicants submit that at least some of the above patents are not appropriate references for an obviousness-type double patenting rejection. In particular, Applicants believe that U.S. Patent Nos. 5,788,956 and 5,932,215 are not be appropriate obviousness-type double patenting references. For instance, Applicants do not believe that the instant invention, directed to treatment of sensitive or capsaicin-sensitive skin via topical application of a substance P antagonist-containing composition, would be obvious in view of the invention of the '956 patent, directed to controlling cutaneous perspiration by applying a substance P antagonist. Additionally, Applicants do not agree that the claimed invention, directed to treating sensitive or capsaicin-sensitive skin via topical application of a substance P antagonist-containing composition, would be obvious in view of the invention

of the '215 patent, directed to treating skin conditions from the group consisting of skin redness, rosacea and discrete erythema by topical application of an effective amount of at least one CGRP antagonist.

However, in an effort to expedite prosecution, Applicants provide appropriate terminal disclaimers for each of the above-cited patents, as attachments to this Response, to obviate these rejections. Applicants submit, however, that by filing of the attached terminal disclaimers, Applicants do not admit to the propriety of these rejections. See M.P.E.P. § 804.02, citing *Quad Environmental Technologies Corp. v. Union Sanitary District*, 946 F.2d 870, 20, USPQ2d 1392 (Fed. Cir. 1991).

Accordingly, reconsideration and withdrawal of the rejections are respectfully requested.

Claims 14-16, 25-28, 32-34, 45-46, 51-52, 55-58, 62-64, 75-76, 85-88, 97, 101, 105-106, 111-112 and 114 stand rejected under 35 U.S.C. §102(b) or §103 as being anticipated by or as being obvious over WO 93/14084. For at least the reasons that follow, withdrawal of these rejections is in order.

Because Claims 2-24 were canceled in the December 14 Request for Filing Continuation/Divisional, Applicants only address rejections of Claims 25-114.

The present invention relates to the use of a substance P antagonist in a composition containing a cosmetically acceptable medium to treat sensitive skin, and to the use of a substance P antagonist to prevent and/or combat skin irritations, desquamation, erythemas, sensations of overheating or of dysesthesia, and/or pruritus in the skin. See specification at page 5, first and second full paragraphs.

For example, independent Claim 25, sets forth a cosmetic or dermatological method for treating sensitive skin of an individual in need of such treatment, such sensitive skin having or developing neurogenic manifestations of dysesthesia caused by the release of substance P therein, the method comprising topically applying to said sensitive skin an effective amount of at least one substance P antagonist-containing composition, and wherein said effective amount of said at least one substance P antagonist is formulated into a topically applicable cosmetically- or dermatologically-acceptable medium therefor.

WO '084 discloses the use of a substance P antagonist as a medicinal and further prophetically discloses that such antagonists may be administered by topical application.

WO '084 does not disclose or suggest each feature of the presently claimed invention. For example, WO '084 does not disclose or fairly suggest a method for treating sensitive skin which comprises topically applying to said sensitive skin an effective amount of at least one substance P antagonist-containing composition, and wherein said effective amount of said at least one substance P antagonist is formulated into a topically applicable cosmetically- or dermatologically-acceptable medium therefor. Instead, WO '084 merely describes specific substance P antagonists and various dosage formulations with no disclosure or suggestion of a cosmetic composition containing the claimed combination.

It would appear, based on the Office Action, that the Examiner is of the opinion that the claims are anticipated or obvious based on the disclosure at page 5 and page 13 of WO '084, wherein topically applicable compositions are mentioned, and the use of such compositions for therapeutic treatment is also mentioned. However, the position of the Examiner is respectfully submitted to be improper.

As discussed above, the reference fails to disclose or suggest the specific method of the invention, namely topically applying to sensitive skin an effective amount of at least one substance P antagonist-containing composition, wherein the effective amount of the antagonist is formulated into a topically applicable cosmetically- or dermatologically-acceptable medium. In addition, WO '084 does not disclose or suggest a method comprising topically applying to sensitive skin or capsaicin-sensitive skin an effective amount of at least one substance P antagonist-containing composition wherein an effective amount of the at least one substance P antagonist is formulated into a topically applicable cosmetically- or dermatologically-acceptable medium. See independent Claims 25 and 85, respectively.

Applicants respectfully submit that the Examiner apparently has ignored, or at least has not accorded sufficient weight to this specific combination which is a requirement of all the claims. Also, the Examiner seemingly does not give sufficient weight to the fact that the claims require a specific combination which is comprised in specific relative ratios (amounts effective to treat sensitive skin or capsaicin-sensitive skin) which is also not suggested by the reference.

Moreover, Applicants respectfully note that the Examiner has included many of the dependent claims in the §102(b) and §103 rejections, not withstanding the fact that there is also no specific disclosure in the reference relating to more specific embodiments of the invention defined in the dependent claims. For example, with respect to Claims 47-50, 77-80 and 107-110, the cited WO publication further fails to disclose or suggest the specific combination of a substance P antagonist, and an active ingredient selected from the group

consisting of protein, protein hydrolyzates, amino acids, polyalcohols, urea, allantoin, sugars, sugar derivatives, vitamins, hydroxy acids, retinol, tocopherol, ceramides, essential oils, and salicylic acid, wherein the active ingredient may result in irritation upon topical application to a subject with sensitive skin (absent the presence of an effective amount of at least one substance P antagonist).

As discussed above, Applicants have carefully reviewed WO '084, including the specific sections of the reference cited by the Examiner. However, Applicants respectfully maintain that the cited WO '084 reference fails to disclose or suggest the subject invention. Applicants acknowledge that the reference suggests that the disclosed substance P antagonists are potentially suitable for use as therapeutics, e.g., for treating irritable bowel syndrome, skin disorders, such as psoriasis, pruritus and sun burn (discussed at page 5, lines 19-20 of the WO '084 disclosure). Similarly, Applicants acknowledge the fact that the reference discloses at page 13 that those substance P antagonists may be provided in a topically administrable composition.

However, the reference does not anticipate or render obvious the claimed invention as it fails to disclose or suggest topically applying to sensitive skin a cosmetic composition containing an effective amount of at least one substance P antagonist-containing composition, as defined in Claims 25, 55 and 85, or topically applying to capsaicin-sensitive skin an effective amount of at least one substance P antagonist-containing composition, as defined in Claim 85. A proper anticipatory or obviousness rejection requires that a reference disclose or suggest all limitations of the claimed invention. Herein, the prior art fails to do so since there is no specific disclosure or suggestion in the

reference relating to a topically administrable composition comprising an effective amount of a substance P antagonist-containing composition, for treating sensitive or capsaicin-sensitive skin, or specifically applying such a composition to sensitive or capsaicin-sensitive skin. To the contrary, the reference merely discloses various substance P antagonist-containing formulations, including topically administrable formulations, and prophetically describes the potential use thereof for treating various disorders, including skin disorders. Therefore, based on the foregoing, withdrawal of the §102(b) and §103 rejections based on WO 93/14084 is respectfully believed to be in order.

Claims 10-16, 18-20 and 24-114 are rejected under 35 U.S.C. §103 as being unpatentable over Wallengren et al. (*Contact Dermatitis*), Wallengren (*BR. J. Dermatitis*) by themselves or in combination with WO 83/01252 and/or WO '084. For at least the reasons that follow, withdrawal of this rejection is in order.

Because Claims 2-24 were canceled in the December 14 Request for Filing Continuation/Divisional, Applicants only address rejections of Claims 25-114.

As explained above, the present invention is directed to the use of a substance P antagonist in a composition containing a cosmetically acceptable medium to treat sensitive skin, and to the use of a substance P antagonist to prevent and/or combat skin irritations, desquamation, erythemas, sensations of overheating or of dysesthesia, and/or pruritus in the skin. See specification at page 5, first and second full paragraphs.

Wallengren et al. (*Contact Dermatitis*) studies the effect of injected substance P in allergic contact dermatitis. Specifically, the reference administers various peptides, including a substance P antagonist, substance P, a vasoactive peptide and somatostatin at

the same site on the skin as the as an antigen in patients exhibiting contact allergy to nickel. In the disclosed experiments, the antigen and the substance P antagonist or other peptide are always separately administered via injection. The authors concluded, based on their results, that "they did not succeed in providing that SP enhances contact Dermatitis." Moreover, not withstanding their prophetic suggestion relating to concomitant administration of the substance P antagonist and the irritant in their experiments, the substance P antagonist and the allergen (nickel sulfate) are always administered separately (via injection). This is evident, e.g., based on the experimental protocol disclosed at page 352, left-hand column of the reference.

Therefore, Wallengren et al. (*Contact Dermatitis*) fails to disclose or suggest topically applying to sensitive skin or capsaicin-sensitive skin an effective amount of at least one substance P antagonist-containing composition for treating sensitive skin or capsaicin-sensitive skin. Rather, Wallengren et al. discloses separately administering a substance P antagonist and a potential irritant wherein the irritant is administered either topically or via injection. Moreover, in all instances, the substance P antagonist is administered via injection. Therefore, Wallengren et al. (*Contact Dermatitis*) fails to disclose or suggest topically applying to sensitive skin or capsaicin-sensitive skin an effective amount of at least one substance P antagonist-containing composition, as claimed. In particular, the reference would not suggest such a method since in all instances the substance P antagonist and the irritant are administered separately, and the substance P antagonist is always administered by injection.

For at least these reasons, the claimed invention would not have been obvious over Wallengren et al. (*Contact Dermatitis*).

Wallengren (*BR. J. Dermatitis*) discloses the injection of a substance P antagonist (i.e., Spantide), prior to challenge with various irritants, i.e., tuberculin, benzoic acid, food allergens, and benzalkonium chloride. The reference further indicates that immunological reactions associated with contact urticaria and reaction to tuberculin were significantly suppressed by injection with the substance P antagonist.

Accordingly, Wallengren (*BR. J. Dermatitis*) fails to disclose or suggest topically applying to sensitive or capsaicin-sensitive skin an effective amount of at least one substance P antagonist-containing composition, as claimed. Rather, Wallengren (*BR. J. Dermatitis*), like Wallengren et al. (*Contact Dermatitis*), discloses separately administering a substance P antagonist and a potential irritant wherein the irritant is administered either topically or via injection. Similarly, in all instances, the substance P antagonist is administered via injection. Therefore, both Wallengren references, taken singularly, fail to disclose or suggest topically applying a substance P antagonist-containing composition to sensitive/capsaicin-sensitive skin, as claimed. In particular, the references would not suggest such a combination since in all instances the substance P antagonist and irritant are administered separately, and the substance P antagonist is always administered by injection.

For at least these reasons, the claimed invention would not have been obvious over Wallengren (*BR. J. Dermatitis*).

The Examiner has recognized the above deficiencies of the Wallengren references but has concluded that the deficiencies of the Wallengren references are overcome by WO

83/01253 and WO 93/14084, which disclose topical application of a substance P antagonist. However, Applicants respectfully traverse this rejection. While Applicants acknowledge that the topical administration of some substance P antagonists has previously been known for treatment of other conditions, topical administration of substance P antagonists has not been known for treating sensitive/capsaicin-sensitive skin or for preventing irritation of otherwise irritant compounds. Therefore, the secondary references do not overcome the above deficiencies of the Wallengren references because they do not reasonably disclose or suggest that a topically applicable composition containing a substance P antagonist would, or even could, treat sensitive/capsaicin-sensitive skin or the irritation normally associated with irritating active agents applied in the presence of such substance P antagonist. To the contrary, as discussed in the subject application, this is a highly surprising discovery. Therefore, based on the foregoing, withdrawal of the §103 rejection based on the Wallengren references, either alone or in combination with WO 83/01252 and/or WO 93/14084, is respectfully requested.

Moreover, Applicants, in a separate Information Disclosure Statement, bring to the attention of the Examiner, various references not previously considered. In this regard, many of these references are cumulative to references already of record.

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited.

If there are any questions concerning this paper or the application in general, the Examiner is invited to telephone the undersigned at the Examiner's earliest convenience.

Respectfully submitted,

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Attachment to Amendment Pursuant to 37 C.F.R. §1.116 dated November 5, 2001

Marked-up Claims 25, 47-48, 55, 77, 85 and 107

25. (Amended) A cosmetic or dermatological method for treating [or preventing] sensitive skin of an individual in need of such treatment, such sensitive skin having or developing neurogenic manifestations of dysesthesia caused by the release of substance P therein, the method comprising topically applying to said sensitive skin an effective amount of at least one substance P antagonist-containing composition, and wherein said effective amount of said at least one substance P antagonist is formulated into a topically applicable cosmetically- or dermatologically-acceptable medium therefor.

47. (Amended) The method of Claim 25, wherein said substance P antagonist is administered with at least one active ingredient selected from the group consisting of protein, [and] protein hydrolyzates, amino acids, polyalcohols, urea, allantoin, sugars, [and] sugar derivatives, vitamins, hydroxy acids, retinol, tocopherol, ceramides, essential oils, and salicylic acid.

48. (Amended) The method of Claim 26, wherein said substance P antagonist is administered together with at least one agent selected from the group consisting of [an agent that affects at least one of skin differentiation, proliferation, and pigmentation,] a skin differentiating modulating agent, a skin proliferation modulating agent, a skin pigmentation modulating agent, vitamin D, an estrogen, an antibacterial agent, an antiparasitic agent, an

Attachment to Amendment Pursuant to 37 C.F.R. §1.116 dated November 5, 2001

Marked-up Claims 25, 47-48, 55, 77, 85 and 107

antifungal agent, an anti-inflammatory agent, an anesthetic agent, an anti-pruriginous agent, an antiviral agent, a keratolytic agent, an anti-free radical agent, an anti-seborrhea agent, an anti-dandruff agent, and an anti-acne agent.

55. A cosmetic of dermatological method for treating [or preventing]sensitive, but not allergic, skin of an individual in need of such treatment, such sensitive skin having or developing neurogenic manifestations of dyesthesia caused by the release of substance P therein, the method comprising topically applying to said sensitive skin an effective amount of at least one substance P antagonist-containing composition, and wherein said effective amount of said at least one substance P antagonist is formulated into a topically applicable cosmetically- or dermatologically-acceptable medium therefor.

77. (Amended) The method of Claim 55, wherein said substance P antagonist is administered with at least one active ingredient selected from the group consisting of protein, [and] protein hydrolyzates, amino acids, polyalcohols, urea, allantoin, sugars, [and] sugar derivatives, vitamins, hydroxy acids, retinol, tocopherol, ceramides, essential oils, and salicylic acid.

85. (Amended) A cosmetic or dermatoligical method for treating [or preventing] capsaicin-sensitive skin of an individual in need of such treatment, such sensitive skin

Attachment to Amendment Pursuant to 37 C.F.R. §1.116 dated November 5, 2001

Marked-up Claims 25, 47-48, 55, 77, 85 and 107

having or developing neurogenic manifestations of dysesthesia caused by the release of substance P therein, the method comprising topically applying to said capsaicin-sensitive skin an effective amount of at least one substance P antagonist-containing composition, and wherein said at least one substance P antagonist is formulated into a topically applicable cosmetically- or dermatologically-acceptable medium therefor.

107. (Amended) The method of Claim 85, wherein said substance P antagonist is administered with at least one active ingredient selected from the group consisting of protein, [and] protein hydrolyzates, amino acids, polyalcohols, urea, allantoin, sugars, [and] sugar derivatives, vitamins, hydroxy acids, retinol, tocopherol, ceramides, essential oils, and salicylic acid.